

**DETAILED ACTION**

***Claims and Previous Rejections Status***

1. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.
2. Claims 1-20 and 36 are pending in the application. Claims 21-35 were canceled in the response filed 4/5/10.
3. The rejection of claims 12 and 13 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.
4. The rejection of claims 1-4,11,15-20 and 36 under 35 U.S.C. 102(b) as being anticipated by Glajch et al. (US 6,455,024 B1) is withdrawn.
5. The rejection of claims 1-5,8,10-16,18-20 and 36 under 35 U.S.C. 103(a) as being unpatentable over Glajch et al. (US 6,455,024 B1) in view of Day et al. (US 5,011,797) is withdrawn.
6. Claims 1-5,8-11,13-16,18-20 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glajch et al. (US 6,455,024 B1) in view of Gilchrist et al. (US 6,143,318) is withdrawn.
7. The rejection of claims 1-4,6,7,11-13,15-20 and 36 under 35 U.S.C. 103(a) as being unpatentable over Glajch et al. (US 6,455,024 B1) and in view of Wong et al. (US2004/0131543A1) is withdrawn.

***Specification***

8. The amendment to the specification filed 4/5/10 is acknowledged.

***New Grounds of Rejection***

***Claim Rejections - 35 USC § 103***

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 1-5,8,10-16,18-20 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glajch et al. (US 6,455,024 B1) in view of Brow et al. (J. Non-Crystalline Solids 1990, 120, 172-177) and Yashchishin et al. (Glass and Ceramics 1997, 54, 6-8) and in further view of Day et al. (US 5,011,797).

11. Glajch et al. (US 6,455,024 B1) discloses a particle/implant which is in a glass state and is comprised of silicas, phosphates, etc., such as calcium phosphate (column 1, lines 8-16; column 5, lines 12-25 and 55-60) and radionuclides, such as <sup>90</sup>Y, <sup>32</sup>P, <sup>33</sup>P, <sup>90</sup>Sr (column 3, lines 22-35; column 5, lines 62+; examples 1-4). The inorganic particles/base glass of the disclosure can be prepared with a range of different solubilities in aqueous fluid, such as body fluid. The solubility of the inorganic particles/base glass of the disclosure may affect the rate of biodegradation (column 6, lines 30-45).

12. Further, the phosphate glass may incorporate up to 12 wt % nitrogen and the radionuclide may be distributed substantially uniformly throughout the inorganic material. The radionuclide of interest may be contacted with the particle via co-

precipitation and therefore does not need or require high energy particle irradiation to convert one or more stable isotopes into radioactive isotopes (column 3, lines 22-35; column 4, lines 65-67; column 5, lines 45-53; column 9, lines 19-28). Co-precipitation is the process in which the radionuclide in a soluble form is intimately mixed with a soluble precursor of the inorganic material. The radionuclide and the inorganic materials are made to concurrently precipitate by means of changing the solvent, adding a precipitating solvent in which the radionuclide and inorganic materials are not soluble, etc. (column 9, lines 56-62). The particles of the disclosure are encapsulated within a biocompatible material/nonconductive delivery vehicle, such as polyethylene terephthalate (PET) and may be used for the method of treating a tumor (i.e. brachytherapy) (column 1, lines 9-16; column 4, lines 9-14 and 47-50). The implants may be administered parenterally (column 1, lines 8-16).

13. Glajch et al. does not disclose the total radioactivity of the isotopes.
14. Glajch et al. discloses that the amount of radionuclide present in terms of wt % will depend on a number of issues: radionuclide chosen, amount of radioactivity required, etc. and can be calculated to provide for the activity required to treat a given tumor volume (Glajch et al. column 6, lines 14-28). Therefore, at the time of the invention it would have been obvious to one skilled in the art to provide the particles/implants in an amount effective of a radionuclide for radiation therapy of a tumor, such as curies of total radioactivity since Glajch et al. teaches that the particles/implants are used for the method of treating a tumor.

15. The calcium phosphate glass particles/implants of Glajch et al. encompasses the calcium phosphate resorbable implant of the disclosure and thus are capable of the same functions and have the same properties, such as calcium to phosphate ratio from about 0.33 to about 1.67.

16. Glajch et al. does not disclose a nitrogen layer on the surface of the particle/implant.

17. Brow et al. (J. Non-Crystalline Solids 1990, 120, 172-177) discloses surface nitridation of a phosphate glass to improve chemical durability and decrease aqueous dissolution rates (p172, Introduction; p176, Conclusion). Nitrogen is incorporated into the phosphate glass surface, from approximately 2 to 8 at. %, via exposure to dry ammonia at temperatures near  $T_g$  (p172, Introduction; p173, Experimental procedure, paragraph 3; p174, results, paragraph 1; p175, first full paragraph).

18. Yashchishin et al. (Glass and Ceramics 1997, 54, 6-8) discloses surface nitrogen doping of phosphate and borate glasses and that just a few weight percent of nitrogen will suffice to bring about a marked improvement in the properties of a glass, such as the chemical stability (by 3 to 6 times), mechanical strength, etc. The surface layer of the glass is modified to a depth that would not change the chemical composition of the glass but enhances the chemical stability and other properties of the glass (abstract; p6, paragraph 3). The glass surface should preferably be doped with nitrogen, and this can be done if the treatment with ammonia is done at a temperature below its softening point, such as from 400-500°C for 0.5-3 h (p6, right column; p8, left column).

19. At the time of the invention it would have been obvious to one ordinarily skilled in the art to dope the phosphate glass of Glajch et al. via the method of Brow et al. and/or Yashchishin et al. to generate a nitrogen layer on the surface of the phosphate glass to improve its chemical stability (by 3 to 6 times), mechanical strength, etc. without changing its chemical composition.

20. Glajch et al. does not disclose the use of the particle/implant for radiation therapy of a tumor or for radiation synovectomy of arthritic joints.

21. Day et al. (US 5,011,797) discloses novel biodegradable and biologically compatible glass microspheres, such as lithium silicates, etc. for radiation synovectomy of arthritic joints which comprises a radionuclide, such as samarium-153 (column 1, lines 9-13; column 8, lines 25-38).

22. At the time of the invention it would have been obvious to one ordinarily skilled in the art that the silicate particles of Glajch et al. are capable of providing an amount effective of a radionuclide for radiation synovectomy of arthritis as the disclosures of Glajch et al. and Day et al. are drawn to the same utility, such as silicate glass particles comprising radionuclides.

23. Claims 1-5,8-11,13-16,18-20 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glajch et al. (US 6,455,024 B1) in view of Brow et al. (J. Non-Crystalline Solids 1990, 120, 172-177) and Yashchishin et al. (Glass and Ceramics 1997, 54, 6-8) and in further view of Gilchrist et al. (US 6,143,318).

24. Glajch et al. (US 6,455,024 B1) discloses a particle/implant which is in a glass state and is comprised of silicas, phosphates, etc., such as calcium phosphate as well as that stated above.
25. Glajch et al. does not disclose a nitrogen layer on the surface of the particle/implant.
26. Brow et al. (J. Non-Crystalline Solids 1990, 120, 172-177) discloses surface nitridation of a phosphate glass to improve chemical durability and decrease aqueous dissolution rates as well as that stated above.
27. Yashchishin et al. (Glass and Ceramics 1997, 54, 6-8) discloses surface nitrogen doping of phosphate and borate glasses and that just a few weight percent of nitrogen will suffice to bring about a marked improvement in the properties of a glass, such as the chemical stability (by 3 to 6 times), mechanical strength, etc. as well as that stated above.
28. At the time of the invention it would have been obvious to one ordinarily skilled in the art to dope the phosphate glass of Glajch et al. via the method of Brow et al. and/or Yashchishin et al. to generate a nitrogen layer on the surface of the phosphate glass to improve its chemical stability (by 3 to 6 times), mechanical strength, etc. without changing its chemical composition.
29. Glajch et al. does not disclose the inclusion of selenium.
30. Gilchrist et al. (US 6,143,318) discloses that soluble phosphate glasses are biocompatible and can incorporate inorganic metals such that a sustained release of the metals can be provided at a wound site (column 1, lines 25-37) or that selenium may be

included into controlled release glasses to provide a bactericidal benefit to promote wound healing (abstract; column 1, lines 46-63).

31. At the time of the invention it would have been obvious to one skilled in the art to include selenium in a glass phosphate implant, such as that of Glajch et al. to provide a bactericidal benefit at the implantation site of the particles/implants of Glajch et al. as both disclosures are drawn to the same utility, such as biocompatible resorbable phosphate glass implants.

32. Claims 1-8,10-20 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Glajch et al. (US 6,455,024 B1) in view of Brow et al. (J. Non-Crystalline Solids 1990, 120, 172-177) and Yashchishin et al. (Glass and Ceramics 1997, 54, 6-8) and in further view of Wong et al. (US2004/0131543A1).

33. Glajch et al. (US 6,455,024 B1) discloses a particle/implant which is in a glass state and is comprised of silicas, phosphates, etc., such as calcium phosphate as well as that stated above.

34. Glajch et al. does not disclose a nitrogen layer on the surface of the particle/implant.

35. Brow et al. (J. Non-Crystalline Solids 1990, 120, 172-177) discloses surface nitridation of a phosphate glass to improve chemical durability and decrease aqueous dissolution rates as well as that stated above.

36. Yashchishin et al. (Glass and Ceramics 1997, 54, 6-8) discloses surface nitrogen doping of phosphate and borate glasses and that just a few weight percent of nitrogen

will suffice to bring about a marked improvement in the properties of a glass, such as the chemical stability (by 3 to 6 times), mechanical strength, etc. as well as that stated above.

37. At the time of the invention it would have been obvious to one ordinarily skilled in the art to dope the phosphate glass of Glajch et al. via the method of Brow et al. and/or Yashchishin et al. to generate a nitrogen layer on the surface of the phosphate glass to improve its chemical stability (by 3 to 6 times), mechanical strength, etc. without changing its chemical composition.

38. Glajch et al. does not disclose an image enhancing agent, such as gadolinium.

39. Wong et al. (US2004/0131543A1) discloses particles/microsphere radiopharmaceutical macroaggregates comprising a metal and one or more radioactive isotopes and which have sufficient radioactivity (p2, [0014]). The particles may be glass microspheres where the non-radioactive metal (i.e. Ca or Gd) and one or more radioactive isotopes are adsorbed by the glass material (p2-3, [0017]). The microsphere radiopharmaceutical macroaggregates are used for MRI, methods for the locoregional treatment of abnormal tissue (i.e. tumor, synovial tissue) and for acupuncture therapy of rheumatoid arthritis (p3, [0018] and [0022]; p4, [0037]; p10, [0076]; p11, [0079]). The microsphere radiopharmaceutical macroaggregates are prepared via coprecipitation of phytate (Inositol hexaphosphate) a non-radioactive cation, a radionuclide cation ( $^{90}\text{Y}$ ) and a radionuclide anion ( $^{99\text{m}}\text{Tc}$ ) (p6, [0053]). The radiopharmaceutical macroaggregates have radioactivity levels of about 1 microcurie to about 500 mCi (p8, [0064]).



40. At the time of the invention it would have been obvious to one ordinarily skilled in the art to include a metal, such as gadolinium as taught by Wong et al. in the glass particle/implant of Glajch et al. for the advantage of allowing for the accurate measurement of geographical distribution of the particles/implants in the injected and surrounding tissues (Wong et al. p2, [0015]) as both disclosures are drawn to the same utility, such as the treatment of a abnormal tissue, tissue, tumor, etc.

### ***Conclusion***

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELISSA PERREIRA whose telephone number is (571)272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/  
Supervisory Patent Examiner, Art Unit 1618

/Melissa Perreira/  
Examiner, Art Unit 1618